IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Jay A. Goldstein, Michael Rothman, and Whe-Yong Lo		
Serial No.:	10/691,928	Art Unit:	1616
Filed:	October 23, 2003	Examiner:	Nathan W. Schlientz
For:	*ANTIFUNGAL FORMULATIONS*		

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Commissioner for Patents
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REQUEST FOR REHEARING

Sir:

Appellants and the undersigned respectfully request reconsideration of the decision relating to obviousness, specifically whether claims 1-3 and 7-17 are obvious over U.S. Patent No. 6,075,056 to Quigley *et al.* ("Quigley").

Remarks

Summary

Quigley does not disclose or suggest selecting low to low-medium steroid formulation to effectively treat fungal infections while avoiding local side effects. In fact, Quigley teaches away from the claimed methods by clearly demonstrating a preference for high potency steroid formulations. As noted by the Board, the claims are novel over Quigley in part because Quigley teaches a preference for high potency formulations, both in the prophetic examples and the

working examples. The Board concluded that one of ordinary skill in the art would need to pick and choose from the disclosure of Quigley to arrive at the claimed methods, which makes the claimed subject matter novel. The same conclusions support a finding of non-obviousness. The only way one can arrive at the claimed methods from Quigley is to ignore those parts of Quigley that teach away from the claimed methods and use the Applicants claims as a road map to pick and choose the relevant portions of Quigley. This is improper hindsight. Therefore, for at least the reasons discussed below, claims 1-3 and 7-17 are not obvious over Quigley.

The working examples in Quigley teach away from low to low-medium steroid formulations

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.* 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant. See *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966), as cited in *In re Gurley*, 27 F.3d 551, 31 U.S.P.Q.2d 1130 (Fed. Cir. 1994).

REQUEST FOR REHEARING

In the Decision mailed on November 22, 2011, the Board of Patent Appeals and Interferences ("the Board") found that 1 and 8-13 were novel over Quigley. In reaching its decision, the Board stated "... (4) Quigley's examples containing 0.064 wt% betamethasone dipropionate appear to be more potent than the claimed compositions." *See* Board's decision, page 3, 2nd paragraph. However, the Board failed to address the fact that these more potent formulations teach away from the claimed methods, a point explicitly raised by the Applicants and the undersigned during the oral hearing on October 18, 2011, and which supports a finding of non-obviousness.

Quigley discloses that "the invention relates to stable topical formulations comprising a non-imidazole bearing anti-fungal agent (i.e., lacking an imidazole functional group within the molecule)... [T]he topical formulation also comprises an antiinflammatory steroid, for example betamethasone, betamethasone dipropionate, fluocinonide, fluocinolone acetonide, hydrocortisone, methylprednisolone, clobetasol, beclomethasone, and the like...[T]he combination has unexpected advantages... [A]nother advantage of the formulation is that it delivers the antifungal agent and the steroid to the skin, but minimizes the penetration of the skin with respect to the steroid, thus avoiding the potential side effects attendant upon prolonged steroid use." *See* col. 1, line 65 to col. 2, line 27.

In other words, Quigley suggests that the ability to minimize penetration of the skin is due to the combination of the steroidal anti-inflammatory with a non-imidazole bearing anti-fungal agent and not the potency of the steroid formulation. While the Board alleges that Quigley discloses the same problem to be solved as the present application, it fails to recognize

that the problem is allegedly solved by selecting a particular class of antifungal agents, not by decreasing the potency of the steroid formulation. There is nothing in Quigley that discloses or suggests selecting a low to low-medium potency steroid formulation to effectively treat fungal infection while minimizing local side effects.

In its decision, the Board held that it is an undisputed fact that Quigley teaches using 0.05% desonide and Appellants compositions explicitly include 0.05% desonide. *See* Board's decision, page 6, lines 6-9. Applicants and the undersigned respectfully disagree. The only mention of 0.05% desonide is in the laundry list of 54 steroid formulations provided at col. 4, line 55 to col. 5, line 51. There is no mention of desonide in the prophetic examples or the working examples. The fact that 0.05% desonide is in a long list of steroid formulations is not a teaching or suggestion to select that particular formulation let alone a low to low-medium potency steroid formulation and therefore does not render the claimed methods obvious. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) (The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness). In fact one would not select 0.05% desonide in view of the working examples teaching the use of 0.064% betamethasone dipropionate, which by the Board's own findings, is more potent than the steroid formulations defined in the claims. *See* Board's decision, page 3, 2nd paragraph.

The Board also alleged that Quigley discloses a preference for the steroid betamethasone dipropionate at concentrations within the range recited in Appellants' claims. *See* Board's decision, page 6, lines 12-15. Applicants and the undersigned respectfully disagree. While

Quigley does disclose a preference for betamethasone dipropionate, there is nothing in Quigley which discloses or suggests a preference for a concentration of betamethasone dipropionate that results in low to low-medium potency. It is important to note that concentration is only one factor which determines potency. Other critical factors include the particular steroid and its salt form, the dosage form (e.g., cream, ointment, gel, or lotion), and the presence or absence of particular excipients, such as penetration enhancers.

Quigley describes prophetic examples A-G. All of the prophetic examples describe a steroid concentration range of 0.01-2.5 wt%, a 250-fold range, preferably 0.01 to 0.1 wt%.

Examples A-C describe creams. The list of steroid formulations at col. 4, line 55 to col. 5, line 51 show that creams containing betamethasone dipropionate at a concentration within the broad range and the preferred range are high to medium-high steroids which are more potent than the formulations required by the claims.

Examples D and E describes gels. There is no example of a betamethasone dipropionate gel in the list of formulations at col. 4, line 55 to col. 5, line 51. The list does include a 0.025% betamethasone benzoate gel, classified as a medium-high steroid formulation, which is more potent than the formulations required by the claims.

Example F describes an ointment. The list at col. 4, line 55 to col. 5, line 51 includes two 0.05% betamethasone ointments, which are classified as class 1 and 2 steroids, respectively. These formulations are significantly more potent than the formulations required by the claims.

Example G describes a lotion. The list at col. 4, line 55 to col. 5, line 51 includes a 0.02% betamethasone dipropionate lotion. This concentration is at the very low end of the

preferred concentration described in Example G. However, there is nothing in Quigley which suggests selecting a low to low-medium potency formulation of betamethasone dipropionate.

Of the 7 hypothetical examples in Quigley, only one appears to encompass a low to low-medium formulation of betamethasone dipropionate, and only if one selects a concentration range at the very low end of the preferred range, assuming that the lotion in Example G is identical or equivalent to the lotion referenced in the list at col. 4, line 55 to col. 5, line 51.

Finally, the Board failed to consider the working examples in Quigley when considering the obviousness rejection. The working examples in Quigley clearly show a preference for high potency steroid formulations. All of the working examples use a 0.064% betamethasone dipropionate cream, which according to the list at col. 4, line 55 to col. 5, line 51 would be classified at least as class 3 potency and more likely class 1 or 2 potency, since it contains a higher concentration of betamethasone dipropionate than the creams classified as class 1 and 2 potency steroids.

Moreover, Example 13 compares the percutaneous absorption of Quigley's formulation with Lotrisone cream, a commercially available high potency steroid formulation which contains the same steroid, salt, concentration, and dosage form as Quigley's formulation. Example 13 alleges that replacing the azole anti-fungal agent clotrimazole with the non-azole antifungal agent butenafine reduces percutaneous absorption. In view of Example 13, one of ordinary skill in the art would be motivated to substitute a non-azole anti-fungal agent for an azole anti-fungal agent and combine it with a high potency steroid formulation to achieve the desired activity sought in Quigley, not select a low to low-medium potency steroid formulation.

Contrary to the Board's conclusion, the Board has failed to show that Quigley has a preference for the steroid potencies required by the claims. While there may be some overlap in concentrations; that does not means the formulations have the same potency. This is clearly demonstrated in the list at col. 4, line 55 to col. 5, line 51 which shows that the particular steroid, the particular salt, the concentration and the dosage form determine the potency of the formulation. One of ordinary skill in the art, reading Quigley, would be led on a path divergent from the one Applicants have taken since Quigley teaches a preference for high to high-medium potency formulations.

In order to arrive at the claimed methods, one of ordinary skill in the art is required to make multiple selections including steroid, salt form of the steroid, concentration, and dosage form. The only way one can make these selections, in view of the disclosure of Quigley, is to use the Applicants claims as a road map to pick and choose the relevant portions of Quigley while ignoring the portions of Quigley that teach away from the claimed methods. This is improper.

The results presented in Dr. Goldstein's declaration are unexpected

The results presented in Dr. Goldstein's declaration are unexpected to one of ordinary skill in the art because Quigley fails to teach or suggest selecting a low to low-medium potency formulation to effectively treat fungal infections while avoiding local side effects. As discussed above, the fact that the laundry list of steroid formulations at col. 4, line 55 to col. 5, 51 includes low to low-medium potency formulations is not a teaching or suggestion to select such a formulation, particularly when the reference as whole clearly shows a preference for high to

medium-high potency formulations. The alleged benefits cited by Quigley are due to the combination of a high to medium-high potency steroid with a particular class of antifungal agent, not by selecting a low to low-medium potency formulation. Moreover, the data presented in Dr. Goldstein's declaration show the efficacy of several low to medium-low potency steroids and thus in commensurate in scope with the claims.

Allowance of claims 1-3 and 7-17 is respectfully solicited.

Respectfully submitted,

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